ANNUAL REPORT

OF

THE HOWE LABORATORY OF OPHTHALMOLOGY

HARVARD MEDICAL SCHOOL

AT THE

MASSACHUSETTS EYE AND EAR INFIRMARY

1968

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Ophthalmic Heritage

Frederick Herman Verhoeff*

In Memoriam

Fig. 1. — Dr. Verhoeff in the Howe Laboratory during the middle 1930's.

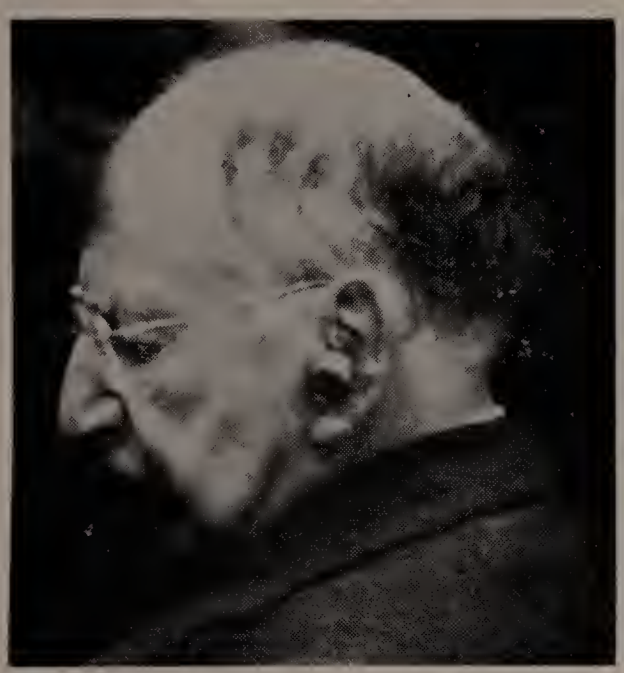

Fig. 2. — Dr. Verhoeff in the early 1960's while attending a meeting of the Wilmer Alumni Association.

On Oct. 22, 1968, Frederick Herman Verhoeff, MD, died at the age of 94. Thus ended the life of one of ophthalmology's dominant figures of this century and seemingly ended also an era of its great individualists. Dr. Verhoeff almost alone established ophthalmic pathology in this country, goaded clinical ophthalmology into a science, and set a unique pattern for overt skepticism and uncompromising honesty. What ophthalmology stands for today bears a distinct Verhoeff stamp.

Born in 1874, Frederick Herman Verhoeff was the son of a prosperous merchant of Louisville, Ky, and the grandson of a Dutch immigrant who had fought under Blücher in the Battle of Waterloo. With the respect for innovations that was to characterize his later life the young Verhoeff was proud that his father was the first one south of the Ohio River to build a grain elevator. But his own preoccupation as a boy was with cameras rather than with business and at the age of 12 he was already

* Part of this summary is taken from an article published by the author in the Harvard Medical School Bulletin, 1962.

marked as an experimentalist in optics. While still in secondary school he decided on ophthalmology as a career. Accordingly he attended the Sheffield Scientific School of Yale because it offered the best premedical course in biology, and then he went on to Johns Hopkins Medical School to graduate with the class of 1899. This was the third class of the new Hopkins School and Dr. Verhoeff, always alert to "firsts," was the first ophthalmologist to graduate from that institution.

By the time of his graduation from medical school, Dr. Verhoeff had already published a paper describing a new instrument for measuring heterophoria and had submitted his paper describing the astigmatic charts which are still in common use today. The former was also presented as an invited communication before the prestigious American Ophthalmological Society!

The interest in optics attracted the young graduate to Dr. Theobald, then head of ophthalmology at Johns Hopkins, but there is no evidence that Dr. Verhoeff planned any formal training in ophthalmology nor had he more than a casual interest in pathology. But as so often happens with one's destiny, a wholly fortuitous association shaped the entire course of his subsequent life. The young Verhoeff happened to be living in the same rooming house as that Hopkins bachelor professor of pathology, Dr. "Popsy" Welch, and it also happened that one of Dr. Welch's students, Dr. Councilman of the Harvard Medical School, was searching for a fulltime pathologist at the Massachusetts Charitable Eye and Ear Infirmary. Dr. Welch suggested Dr. Verhoeff for the position. That Dr. Verhoeff had not had much experience in pathology did not seem to matter. Welch said he could learn it as he went along. And so he did, joining the Infirmary's staff in 1900 and gradually becoming America's most distinguished ophthalmic pathologist.

Verhoeff's reception in Boston was not one of unadulterated cordiality; nor was his salary of $650 particularly munificent. In the first place, the clinical staff had unsuccessfully attempted to do their own pathology, and reform measures are not known to engender benevolence. We are told that Dr. Verhoeff's uncompromising forthrightness seemed contumacious to his clinical peers.

His functions bore little semblance to what is expected of a comparable pathologist today. Not only did Verhoeff do the autopsies (because deaths from ear and sinus infections were then frequent) and make the definitive diagnoses, but he had to do all the sectioning, staining, mounting of slides and preparation of solutions himself. He was a bacteriologist as well as a pathologist. He also did the photography, and when projection equipment was not available he made his own. When the apparatus needed repairing, he did it himself. (Once he developed mercury poisoning after repairing a thermostat on the sterilizer. Apparently mercury had been spilled in the vicinity of a hot air vent near his microscope.) He had no secretary and wrote all the reports by longhand or typed them on his own typewriter.

Verhoeff learned not only eye and ear pathology but he proved to himself his interest in ophthalmology and proved to others his unique qualities. After two years of this baptism by fire, he went abroad for the customary schooling on the continent and there studied with such

persons as Fuchs in Vienna, Haab in Zurich, and Parsons in London. He was to be their counterpart in America.

In 1907, some time after his return to Boston, a pathology laboratory was constructed at the Infirmary according to his design. Here a series of studies in eye pathology began, and a center for training ophthalmic pathologists was instituted that continued with the Verhoeff stamp until 1932 when he resigned to become Director of the Howe Laboratory. It would be hard to say whether the most significant consequence of this quarter century of the Infirmary's "Path Lab" was the stream of practical observations, the host of trainees, or the image created by Verhoeff of intellectual honesty and aversion to hypocrisy.

During this period Dr. Verhoeff became a clinician and surgeon of distinction as well as a pathologist. He proved the mutual fruition of ophthalmic practice and ophthalmic pathology. His name is attached to surgical instruments and ophthalmic procedures as much as it is to elastic tissue stains and methods of eye pathology.

His interest in optics continued and, relieved of his duties as pathologist, he returned more vigorously than ever to his interests in binocular vision and stereopsis. To some of us his *Theory of Binocular Vision*, published in 1935, is a creed.

Retired from his active academic post at Harvard as Professor of Ophthalmic Research in 1940, Dr. Verhoeff began an active clinical practice in his office on Commonwealth Avenue. This he continued until ill health forced his retirement at the age of 85. He continued to attend many medical meetings, including the annual meeting of the Ophthalmic Pathology Club in Washington, DC (which in 1962 became the Verhoeff Society) and participated in the discussions with typical Verhoeff vigor. Deafness and poor vision together with transportation problems made the effort of conference attendance increasingly difficult and at the age of 92 Dr. Verhoeff regretfully discontinued active participation in affairs at the Infirmary. Yet he maintained an alert interest in both scientific and personal happenings and he obviously appreciated reminders of his past associations. He suffered for several years from angina, the first attack having occurred at a meeting of the Verhoeff Pathology Society, and up until the few days just prior to his death he was characteristically experimenting with new forms of medicine for it. When in 1966 he developed a central scotoma consequent to an occluded retinal vein, he published his last paper describing the nature of after-images in the presence of a scotoma. A scientific paper reporting original observations at the age of 92 must come close to establishing a record. It may be that this paper by reason of its being a publication at this age may be another "first" in the ophthalmic literature.

Those of us who knew and worked with Dr. Verhoeff developed a highly personal attachment to him. We knew he was not always right, but we knew his evidence was firsthand, and we respected his logic. We took no offense at his satire because we knew it was so often warranted. We also knew that even when he was castigating us he had the same fondness for us that we had for him. He may have appeared egocentric at times but this is probably a necessary quality of the creative scientist, and Dr. Verhoeff was too honest to hide it. He was not born to the age

of bon mots and polite gloss. He did not indulge in them himself — feeling that to do so would be perjury — but he was often victimized by them. He may have been led to believe things which others said in the manner of social parlance. Once after a particularly lavish panegyric he was moved to say that he considered himself most unworthy of the eulogy. He knew he was ignorant; but others were just more so.

Those of us who knew him well considered him a most humble person. Rarely has one in a comparable position of authority sought out and accepted contrary opinions of interns, residents, and students. As had William Beaumont 150 years before, Verhoeff considered himself a "humble enquirer after truth." More often than not, those who were the butt of his criticism had deviated from the truth. He had little use for secondhand opinions or unsupported dogma. The only real authority for Dr. Verhoeff was truth as revealed through direct observation.

It was no doubt of just such men as Dr. Verhoeff that Sir Henry Wotton wrote in an earlier time:

> How happy is he born and taught
> That serveth not another's will;
> Whose armour is his honest thought,
> And simple truth his utmost skill!

David G. Cogan, MD

The history of the Howe Laboratory and the influence of its former Director, Dr. Frederick H. Verhoeff, are so intertwined that we are including with this Annual Report an obituary commemorating his life which ended on October 22, 1968, at the age of 94. It may be recalled that the Laboratory was founded at the Harvard Medical School by Dr. Lucien Howe in 1927. But Dr. Howe, its first Director, lived only a few months after the founding, and it was not until 1932, when the Laboratory's location was transferred to the Massachusetts Eye and Ear Infirmary and when Dr. Verhoeff was appointed Director, that the Laboratory became an active organization. In his eight years as Director and in the subsequent many years as unofficial counsellor to the Laboratory, Dr. Verhoeff imparted the characteristic stamp of intellectual curiosity and scientific integrity. We are all saddened by his passing but his pervasive influence continues a rich legacy for the Howe Laboratory.

GLAUCOMA

Drug Effects

As Director of the Glaucoma Consultation Service, Dr. Grant has had the opportunity to direct and collaborate in many clinical projects this past year. Some were aimed at determining the safe limits of drugs in common usage, some at discovering new pharmacologic means for treatment of glaucoma and some at devising new surgical approaches. Dr. Grant's collaborators have been Residents, Fellows and Staff of the Massachusetts Eye and Ear Infirmary.

Popular apprehension about the use of vasodilators by patients with open-angle glaucoma or threatened angle-closure glaucoma prompted the evaluation of these drugs by Drs. Peczon, Grant, Lambert and Aquino. Nicotinic acid and cyclandelate were found to cause no rise in the intraocular pressure. Inhalation of carbon dioxide and oxygen caused only a small and transient rise. Oral use of atropine in customary therapeutic doses was also found to cause no acute rise in the intraocular pressure but Drs. Lazenby and Reed are continuing their search for possible long-term effects on patients with open-angle glaucoma.

Lens Extraction and Glaucoma

What effect does uncomplicated cataract extraction have on the

control of open-angle glaucoma? Dr. Aquino compared the tensions, tonographic measurements and gonioscopic findings in a group of glaucomatous patients before and after their cataracts were removed. During the first six post-operative months the tensions were more easily controlled in a considerable proportion of patients due to reduced formation of aqueous humor. But this advantage decreased progressively thereafter. It occasionally happens (5 cases in the present series) that the glaucoma is permanently cured by lens extraction through either the incidental formation of a draining bleb at the wound site, or, more commonly in the present series, through the fortuitous formation of a direct opening into Schlemm's canal.

Malignant Glaucoma

Malignant glaucoma is a special condition which is notoriously refractory to both medical and surgical attempts at treatment and has devastating effects on the eye. Drs. Chandler, Simmons, and Grant reported their experience in 24 patients, in approximately half of whom the malignant glaucoma was controllled by new medical methods including mydriatic-cycloplegic treatment. For the other half, in whom operation was necessary, significant improvements in the procedures have been made to render the required surgery simpler and safer. As a result, malignant glaucoma is now less malignant.

Tonometry

Comparison of Schiotz and applanation tonometry, a long term project of Dr. Grant, has had the assistance this year of Dr. Anderson in analyzing the data on 906 patients who have had tonometry done by both methods and with a variety of different tonometers. The tests are done with the patients in the recumbent position so as to maintain similar conditions of measurement and the results are compared with measurements by applanation in the sitting position. The data are being analyzed with the assistance of computer technology and should provide information on the variability in tensions recorded with multiple tonometers of the same type, with different types of tonometers, and under different conditions of the patients.

Information System

It should also be noted that Dr. Grant has been experimenting with and developing an information system especially for glaucoma and another system particularly for toxicology of the eye. These systems have already shown their usefulness in providing needed information promptly, and will be highly specialized adjuncts to the broader coverage of the ophthalmic literature (see description of Vision Information Center).

HISTOPATHOLOGY

Retinal Damage by Excessive Exposure to Light

In the Annual Report of two years ago we noted the observations of Drs. Kuwabara and Robert Gorn on damage to the retina by continuous exposure to light. Rats exposed to intensities of 1000 foot candles (about 1/10th the intensity of out-door sunlight) had a decreased electroretinographic response after a few hours of exposure and became irreversibly blind within a week. The minimal morphologic changes, possibly representing a physiologic process, consisted of vacuolation in the lamellar plates at the outer tips of the photoreceptors, whereas the severe changes, associated with irreversible blindness, consisted of loss of the entire photoreceptive end organ. Further observations with Mr. Kenneth Stampfer, a medical student, have now shown that the pigment epithelium behind the retina accumulates lamellar bodies concomitant with the exposure to light. These bodies or cellular inclusions appear to come from breakdown products of the outer segments of the photoreceptors.

The relevance of these observations to man is open to question. One of the brightest lights to which man is exposed is that of the indirect ophthalmoscope. Drs. Ephraim Friedman and Kuwabara did, in fact, find that prolonged exposure of the monkey eye to this light caused considerable damage to the retina and pigment epithelium. The experimental conditions were more severe than those employed clinically but have alerted us to potential hazards of prolonged ophthalmoscopy especially in anesthetized patients.

The demonstrated damage to the retinal tissue by extensive exposure to light makes one wonder what role, if any, light may play in the common and enigmatic degenerations of the retina, espe-

cially those of the macula. This is, of course, not a novel question but the foregoing experimental observations give it new poignancy. It was with this in mind that Dr. Cogan took issue this past year in several architectural and public health journals with the excessive amounts of light recommended by some illuminating engineers for libraries and other public buildings. The issue has evoked lively discussion. While we must admit that man does appear to be less susceptible than animals to the harmful effects of light, we suspect, however, that he is more susceptible than is generally believed.

Laser Lesions

The use of laser radiation in the treatment of diabetic retinopathy prompted Drs. Kuwabara and Lloyd Aiello to study its histopathologic effects experimentally. To no one's surprise it was found that discrete destruction of the photoreceptors and contiguous pigment epithelium occurred at the site of exposure. Noteworthy, however, was the prompt replacement by normal cells when the exposure was mild, and most unexpected was the later occlusion of the overlying retinal capillaries, at a time when the outer portions of the retina had returned to normal! This secondary and delayed effect on the retinal capillaries may be the mechanism by which widespread laser irradiation benefits diabetic retinopathy.

Microtubules

Of the many intracellular organelles which have been revealed through the electron microscope, microtubules comprise one of the newest and least understood. Consisting of tubules about 200Å in diameter, there are literally hundreds running parallel to the main axis of certain cells whereas they are absent from other cells. Suggested functions are mechanical support, transfer of nutrients, or conduction of impulses.

Dr. Kuwabara has previously described microtubules in neuronal cells of the retina and noted that they were characteristically absent from glial cells. He has now found them presenting a highly organized pattern in normal lens cells. In the lens epithelium they are sparse and randomly arranged. At the lens equator where the cells differentiate into lens "fibers" the microtubules progressively increase while the other organelles decrease so that in the cortical fibers the microtubules are the only recognizable organelles in an otherwise amorphous milieu. With disintegration of the cell wall

in the center of the normal lens (lenticular nucleus) and in pathologic cortical cells in the process of cataract formation, the microtubules disappear.

The function of these microtubules is far from clear but in the lens there appears to be no need for a conductive mechanism (as there is for instance, in the neurons of the retina). Moreover, the absence of any connection with other organelles makes a metabolic function unlikely. It seems reasonable to infer, therefore, that the microtubules serve a mechanical function, possibly maintaining the form of the lens during the act of accommodation.

Experimental Glaucoma

The effects of experimental glaucoma in monkey eyes produced by the local injection of alpha chymotrypsin has been studied by Drs. Simmons Lessell and Kuwabara. With pressures rising to 30–60 mm Hg, demyelinization of the optic nerve was first evident histologically in two weeks and the ganglion cells gradually disappeared during 2–3 months after the injection. Cavernous atrophy of the optic nerve was not observed in the monkeys. The most striking histopathologic abnormality was a selective degeneration of muscle fibers in the ciliary body although the iris was relatively unaffected.

Miscellaneous Pathologic Studies

Urate crystals were demonstrated by Drs. Harvey H. Slansky and Kuwabara in epithelial scrapings from a patient with *gout*. The crystals had been seen clinically as yellow scintillating particles when viewed with the slit lamp. By photomicroscopy they could be seen within the nuclei of many epithelial cells, but were especially striking in electron micrographs where they presented a characteristic crystalline configuration within the nuclei.

What may be the first description of ocular involvement in *familial lymphohistiocytosis* was reported this past year by Drs. Robert Peterson and Kuwabara. This entity is one of a group of genetic diseases. In the present case massive accumulation of lymphocytes and large histiocytes were formed in the vitreous, retina, uvea, and optic nerves. It was the presence of these cells in the anterior chamber which had given rise to a clinical impression of uveitis.

Ocular *pemphigus* was studied at the microscopic and ultra-

microscopic level by Drs. Carroll and Kuwabara. In this disease there is an abnormally firm adhesion of conjunctival cells to each other. The electron microscopic explanation of this adhesion is an increase in the desmosomes and keratofibrils which, together with the loss of goblet cells, is believed to contribute to the deleterious dryness of the eye in pemphigus.

Dr. Carroll has participated in a collaborative study with Dr. Claes Dohlman and other members of the Cornea Service to evaluate the toxic and adhesive properties of the cyanoacrylic plastics. This material is receiving preliminary trial as an epithelial substitute in otherwise incurable *bullous keratopathy*.

Several cases of *temporal arteritis* have been studied electron microscopically by Drs. Kuwabara and Reinecke. The most striking change at the ultrastructural level was degeneration of the muscle cells and the subsequent breakdown of the muscle cell's product, elastin. After the characteristic giant cells disappeared, the muscle cell generated new elastin in a reparative process.

To emphasize the lessons to be learned from correlating clinical lesions with their pathologic bases, Dr. Thomas Souders and Dr. Cogan have collected for publication photographic material on a *group of diseases* that include keratoacanthoma, molluscum contagiosum, band keratopathy, arcus senilis, cystinosis, temporal arteritis, diabetic retinopathy, and retinal embolization.

The pathology of *diabetes* has been a long-term joint interest of the Howe Laboratory and of the Joslin Clinic (Dr. Merrill Legge). This past year Dr. Bernard Chazan and Dr. Kuwabara reported marked thickening of the basement membrane in conjunctival blood vessels of diabetics. This was unlike the appearance in vessels constricted by adrenalin. Another study of diabetics, conducted by Dr. Marios Balodimos and Dr. Kuwabara, was directed toward determining a possible effect of prolonged sulfonylurea treatment on the retinal blood vessels. No significant difference was found in flat mounts of the vessels from treated patients as compared with a control group.

To test the frequent assertion that patients with *keratoconus* are inordinately subject to various atopic disorders, Dr. Carroll compared the incidence of these disturbances in 30 patients with keratoconus to that in 30 normal individuals. No significant difference was found in the two groups.

BIOCHEMISTRY

Cataracts

Dr. Kinoshita and his collaborators have studied cataracts with an experimental model which results from the feeding of galactose to animals or from incubation of lenses in a galactose medium. The aim of their studies has been to identify the primary factor which initiates the cataractogenic process. The working hypothesis is that conversion of galactose to dulcitol is the mechanism which triggers the process of cataract formation and that all other changes—swelling, formation of vacuoles, loss of amino acids, and electrolyte imbalance—are secondary to the accumulation of dulcitol. The enzyme involved in dulcitol synthesis, aldose reductase, plays a key role in the production of the cataract. It follows that inhibition of this enzyme should prevent cataract formation. To explore this possibility, a cooperative study by Drs. Kinoshita and Jedziniak with Ayerst Laboratories was organized to search out and test inhibitors of aldose reductase. Of the many compounds which have been screened, one inhibitor, tetramethylene glutaric acid (TMG), has been found especially effective in inhibiting galactose cataracts in vitro. Lenses cultured in media containing TMG remain as clear as the normal controls while their counterparts without TMG show characteristic swelling, loss of amino acids, electrolyte disequilibrium, and opacification.

These preliminary observations strongly support the concept that inhibition of the appropriate enzymes may prevent at least this type of cataract.

An electron microscopic study of these experimental galactose cataracts was undertaken by Dr. Kuwabara. In addition to swelling of the lens fibers, vacuoles appeared between the fibers and the aggregate of these vacuoles comprised the early cataracts which could be seen clinically. Later changes consisted of irreversible degeneration and proliferation of the lens cells.

Although galactose cataracts occur in human beings as a result of congenital metabolic defects, the more common form of "sugar cataracts" is that which occurs with the hyperglycemia of diabetes. Drs. Chylack and Kinoshita have therefore explored the pertinence of the foregoing observation on galactose cataracts to glucose cataracts. On incubation of rabbit lenses in high glucose media, a sugar

alcohol (sorbitol) builds up analogous to the dulcitol which develops from galactose in the media. The associated swelling of the lens fibers causes an increased permeability of the membranes and eventually a cataract similar to the galactose-induced cataract. But most significant is the finding that TMG in the medium will practically abolish the accumulation of the sorbitol and also prevent this type of cataract from forming.

The import of these studies is, of course, that aldose reductase plays a primary role in the formation of sugar cataracts and that we have, for the first time, a means for preventing these cataracts. Present efforts are directed toward applying these test tube observations to experimental animals.

Retinal Enzymology

Since congenital defects in the retina, as elsewhere, are commonly caused by deficiency of specific enzymes and since our knowledge of the factors which induce enzyme development is woefully meager, we must pursue any leads contributing to better elucidation of enzyme formation. To this end Dr. Reif-Lehrer has chosen the enzyme glutamine synthetase in the developing chick retina as a model and has searched for a factor in serum responsible for its development. Hydrocortisone appears to fulfill the characteristic of such a factor and to act through an effect on formation of messenger RNA, independent of protein synthesis.

It is a long reach from these studies on the chick retina to enzymology in the human retina and to their application in the clarification of specific congenital defects in infants but that is their ultimate goal. The next logical step, already being pursued, is to develop an appropriate tissue culture of neuronal cells from human retinas in the hope that the cell colonies will maintain and replicate their natural enzyme constituents.

NEURO-OPHTHALMOLOGY

Fluorescein Angiography

When Dr. Haining introduced fluoroangiography to us two years ago we did not anticipate the dimensions it would shortly assume.

Now it occupies most of the full-time facilities of photographer Mr. Lancaster and his staff and the part-time services of Drs. Wray, Guzak, Wurster and Cogan to say nothing of a secretary's service and the demand on space. We have assembled a vast library of angiograms representing various circulatory abnormalities of the retina, choroid, and optic nerve head. These angiograms are now being cataloged and analyzed. Ever mindful of the dangers, however remote, we do not perform the test unless we are convinced of its potential value to the patient. We are not yet persuaded of its routine usefulness but in certain cases it may be the only means of identifying a leak from the blood vessels or in selecting sites for photocoagulation of abnormal blood vessels. It also gives valuable information on the pathogenesis of many disease processes.

An exhibit illustrating some of the abnormalities visualized by fluoroangiography and correlating them with histopathology, prepared by Drs. Wray, Guzak, Cogan and Mr. Lancaster, was awarded

Exhibit of fluoroangiograms prepared for the Fall meeting of the Academy of Ophthalmology and Otolaryngology. The nine foot panels contained illuminated diapositives with a pre-recorded description of each slide for individual listening.

2nd prize at the annual meeting of the American Academy of Ophthalmology and Otolaryngology.

The basis for fluorescence in angiography is being approached experimentally in monkey eyes by Drs. Wray and Anderson. Dr. Wray is studying the luminescence which occurs when fluorescein is injected directly into the eye or behind the eye; Dr. Anderson is studying its appearance in experimentally induced papilledema.

Inborn Metabolic Diseases

With a continuing interest in the inborn metabolic diseases, Drs. Cogan and Kuwabara have summarized current knowledge on the ocular aspects of sphingolipidoses with special emphasis on their own experiences. The diseases included are known by the eponyms of Nieman-Pick, Tay-Sachs, Farber, Krabbe, Fabry, and by the more specific names of generalized gangliosidosis and metachromatic leucodystrophy. We and other investigators have been able to demonstrate storage of abnormal glycolipid in the ganglion cells of the retina in some of the diseases, and involvement of the optic nerve and ocular vasculature in others. In addition to making certain clinical-pathologic correlations, we have had the opportunity to study several cases histochemically and electron microscopically showing in several cases the characteristic accumulation of laminated storage substances (presumably the sphingolipids) in the swollen lysosomes of the retinal ganglion cells. The substance of these studies was presented in the deSchweinetz Lecture at Philadelphia.

Retinal and Papillary Vasculitis

One of the more obscure and certainly one of the more serious diseases which ophthalmologists are called upon to treat is vasculitis of the retina and nerve head. Its importance is only heightened by our ignorance and lack of effective treatment. Hoping to shed some light on this dark corner of ophthalmology, Dr. Cogan reviewed the approximately forty cases in his clinical files and twelve cases in his pathology files. Analysis of these cases did not suggest any one etiologic or histopathologic pattern. Individual cases appeared to be caused by herpes (simplex and zoster), syphilis, allergic reactions and demyelinative diseases. The majority remained without recognized cause appearing idiopathically in young persons as

a primary occlusive vascular disease, often leading to blindness. A report of these cases constituted the MacKenzie Lecture given in Glasgow.

Electrophysiology of the Visual Pathways

The unique system developed by Dr. Fricker for determining signal amplitude and response-conduction time through measurement of electric responses in the retina and occipital lobes after exposure of the eye to flashes of light has found especial usefulness in patients whose visual functions cannot be measured by the usual methods of testing. Thus it is of great value in ocular injuries, in eyes with dense cataracts, as well as in certain neurologic patients, and in babies. When relatively normal signals are obtained, one feels fairly sure in ruling out any gross abnormality. On the other hand, interpretations of abnormal signals are still subject to uncertainties that only further experience will clarify.

Objective Determinations of Stereoscopic Vision

The presence or absence of stereoscopic vision is often important to determine in the evaluation of binocular function. This function is customarily tested by subjective criteria which are often difficult to apply in young children and in others unable to cooperate with subjective observations. For its objective assessment, Dr. Reinecke has developed an ingenious prototype consisting of a random dot stereoscopic pattern which, when visually fused, produces a barber-pole illusion. By rotation of the target about a horizontal axis the barber-pole stripes appear to move from right to left or vice versa so long as the patient has stereopsis. The eye movements are monitored by electro-oculography. A modification of this stereoscopic pattern incorporates an illiterate E which young children may find easier to fuse visually.

Consultative Functions

With interest in neuro-ophthalmology well established in the Howe Laboratory, we have continued to learn from, and have been able to make some contributions to, the large number of neurologic cases which we study in consultation. Most significant perhaps is the full-time attendance of Dr. Shirley Wray who, as a neurologist, can give an evaluation not at the disposal of most ophthalmologists.

She and Dr. Cogan are assisted by residents and by neuro-ophthalmic Fellows who in the past year were Drs. Zweifach and Wurster. The result is a wealth of clinical and research material that is shared through conferences, file searches and clinical consultations.

MICROBIOLOGY

The herpes simplex virus commands a leading interest in ophthalmic investigation because in this country it is the most common cause of ocular infection and of blindness through corneal opacification. This past year Drs. Pavan-Langston and T. Nesburn discovered evidence that the primary infection occurs in the conjunctiva and in the ocular adnexa rather than in the cornea as generally supposed. When virus is inoculated on the uninjured eye of rabbits, it disappears from the surface of the eyes in 4–6 hours. But it can be recovered from the tear film and lacrimal gland in 10–16 hours. Not until 20–24 hours after inoculation can it be recovered from the cornea. The evidence suggests that the corneal epithelium is relatively resistant to infection. But once the eye is infected the virus can be recovered from the cornea for 7–8 days (from the epithelium, stroma, or endothelium) whereas it can be recovered from the conjunctiva and lacrimal gland only for 5–6 days after inoculation.

Less well documented but equally important is the evidence for herpetic cause of uveitis. Not surprisingly the herpes virus has previously been recovered from the anterior chamber of patients with herpetic keratitis. Nor is it surprising that recurrent iridocyclitis (anterior uveitis) has been reported in patients who had had herpetic keratitis. But this past year Dr. Pavan-Langston was able to recover the virus from the anterior chamber of a patient who had bilateral panuveitis and retinitis without history of corneal disease. The patient was a 34-year-old woman who was having a second attack of uveitis coming on post-partum. The uveoretinitis was preceded by blisters on the nose and was characterized by choroidal and retinal exudates. It is believed to be the first case to give positive evidence for a herpetic origin of posterior uveitis.

Equally significant was the disovery, by Dr. Pavan-Langston, of a species of Mycoplasma which causes a nongranulomatous panuveitis in experimental animals. It has been possible not only to

isolate the agent directly from the diseased eye but also to demonstrate a progressive and significant rise in antibody titer to the agent in the serum. This infection is the first experimental model of Mycoplasma uveitis. Clinical and experimental studies are now being undertaken to determine the possible role of this agent in uveal inflammation of man.

OPTICS

Three dimensional photography of the eye, which has been made possible by the Donaldson cameras that are now in various eye centers throughout the world, is being extended to slit-lamp photography. The problem has been to obtain sufficient depth of field to visualize simultaneously the slit and the various portions of the eye illuminated by the beam. Present modifications are now yielding satisfactory results with equipment that can be attached to the existing camera.

Another photographic device has been developed by Dr. Donaldson to record aberrations in the contour and shape of the cornea. The Placido disc, which is customarily used to indicate surface irregularities of the cornea, consists of concentric rings reflected from a limited portion of the corneal surface. Dr. Donaldson's new device permits photography of these rings in a way that will include simultaneously the entire cornea, while maintaining three dimensional visualization. It may be attached to the standard camera and should provide valuable information on the characteristics and course of such conditions as keratoconus.

A first approach to automated refraction was explored by Drs. Brubaker, Reinecke, and Jack Copeland. Computer programs were devised to handle refractive readings from three pre-established meridia (0°, 45°, and 90°) and to read out immediately the sphero-cylindric prescription. Preliminary experience suggests this is an entirely feasible method.

CENTER GRANT ACTIVITIES

Three years ago the National Institute of Neurologic Diseases and Blindness made a substantial grant to support clinical research in the Howe Laboratory and in the Massachusetts Eye and Ear In-

firmary. With Dr. Cogan as responsible-investigator and Dr. Reinecke as administrator, this grant continues to support research in various Departments of the Infirmary (Retina, Cornea, Ocular Motility, Glaucoma, and Neuro-ophthalmology) as well as in some of the clinically oriented and core functions of the Howe Laboratory.

The Center Grant investigations not described elsewhere in this Report because of only tenuous connection with the Howe Laboratory consisted of: alloplastic substitutes for corneal tissue (Dr. Claes Dohlman and collaborators), cryoprobe therapy (Dr. Percy Amoils), illumination system for a goniotomy knife (Dr. Amoils and Richard Simmons), sclerocorneal lenses for a variety of diseases (Drs. Carroll and David Miller), double blind study of retrobulbar neuritis (Drs. William Collis, David Cohen, and David Poskanzer), serial biopsies of temporal arteritis (Dr. Cohen), electronic measurement of eye movements and eye positions (Dr. Fricker), sensitivity profiles of the retina (Drs. Ernst Wolf and Lothar Spillmann), electroretinography in children (Dr. Elliott Berson) and ultrasonography in ocular and orbital abnormalities (Dr. Andrew Dahl).

VISION INFORMATION CENTER

The Vision Information Center (VIC) has been a major undertaking, with Dr. Reinecke at the administrative helm assisted by a group of scientific consultants. Systems of literature retrieval, computerized access to bibliographic sources, and programmed instruction have been developed now which, after three years of experimentation, are beginning to yield results. The VIC was the fourth Information Center to be established by the National Institute for Neurologic Diseases and Blindness and the only one concerned with vision. It has been an expensive investment of federal funds (about a quarter million dollars annually) that can be justified only if it serves a national need. A conjoint responsibility of the Howe Laboratory, the Countway Library (Harvard) and the Infirmary, the Center's specific and ultimate aim is to establish automated electronic connections among all the major medical and ophthalmic libraries of the United States so that all the bibliographic reserves will be immediately accessible to individual users wherever they may be.

The first practical test of a portion of this system was a trial run at the recent meeting of the Academy of Ophthalmology and Otolaryngology. Two consoles were set up in the Exhibition Hall in Chicago connected by telephone lines with the Harvard computer in Cambridge (IBM 360/50) so that references on subjects from a current thesaurus could be obtained automatically within a few seconds. The system has incorporated a conversational mode of

A first public trial of the Vision Information Service was set up in Chicago at the Fall meeting of the Academy of Ophthalmology and Otolarygology. Two typewriter consoles were connected on-line with the Harvard Computer in Cambridge so that physicians could obtain within a matter of seconds bibliographies of articles which had been indexed in the Vision Information Center files.

assisted instructional language which enables the user to ask for appropriate bibliographies while seated at an electronic typewriter either in the Boston area or elsewhere in the United States. A second trial will be in Florida at the meeting of the Association of University Professors early in 1969. The bank of references accumulated from the current literature is now about 4,000 but this is being rapidly expanded and 4,000 journals per month (i.e. the entire

subscription list of the Countway Library) are scanned for articles relating to vision. By the time the electronic mechanisms are "debugged" the system should prove a great boon to the almost overwhelming problem of literature retrieval. Eventually it may supply abstracts and whole articles; this will depend on the future status of library science as much as on our own efforts.

TEACHING AND LEARNING

Non-professional Education

In view of the increasing demand for public information on medical matters, we have been experimenting in recent years with several means of delivering information in a factual and acceptably dignified manner. Fortunately, and perhaps significantly, we have received generous support from the American Contract Bridge League Charity Foundation for this purpose. One film on glaucoma, highlighting the Infirmary's role in treatment and research, was prepared by Dr. Richard Simmons. Another directed to patients with glaucoma has been in the process of development by Dr. Thomas Hutchinson along with his glaucoma "classes" for patients. Drs. Cogan and Wray prepared a video documentation of vascular diseases which has been displayed on a public educational channel. Now, again thanks to the Contract Bridge League, we have purchased television equipment for the immediate recording and play-back of subjects for conference presentations.

Undergraduate Instruction

The participation of the Howe Laboratory staff in undergraduate and postgraduate instruction has always been a source of mutual benefit. It comprises formal lectures, informal conferences and abundant individual consultations. We have no wish to change it except insofar as circumstances dictate. One of these dictations which has concerned us these past few years has been the decreasing time allotted to medical students for ophthalmology and the expressed intent of incorporating specialization earlier in the medical school curricula. It is not impossible, however, that these changes could be beneficial to ophthalmology. Specifically we believe the opportunity now exists as it never did before of formaliz-

ing an undergraduate course for senior medical students who have decided to specialize in ophthalmology.

Accordingly a two month elective course was organized this past year by Drs. Cogan and Alfred Scott and given to 12 senior medical students emphasizing the basic sciences in clinical ophthalmology. In this course we had the active participation of the staffs of the Infirmary and Howe Laboratory. It was a successful experiment, possibly the prototype of other and larger courses if specialization does become an undergraduate discipline.

Postgraduate Instruction

Preceptor training for ophthalmic research has long been one of the major emphases of the Howe Laboratory. The trainees have included those who, in a pre-resident status, have a year or more of exposure to research (perhaps the sole contact of these trainees with laboratory research in their entire careers), those who undertake a sophisticated research project but still are only temporarily attached to the Laboratory, and those who, like the writer, constitute the permanent staff but nevertheless consider themselves perennial trainees. Through its diversity of interests and its proximity to a major hospital, the Howe Laboratory has had an unusual opportunity to pioneer. with mutual give and take, in the supremely important field of ophthalmic research. Dr. Grant supervises that portion of the program which involves the preresident and resident trainees supported by a National Institutes of Health Training Grant.

The efficacy of training cannot be measured as nicely as research output, but the appointments and attitudes of former trainees offer an approximate index. The following comment from a former trainee, received while this Report was in preparation, may be an exaggeration but it is what we would like to believe and what makes us feel our labors are not in vain:

"I find myself very, very humble as well as grateful. For reasons I've never questioned, I was privileged to come to the Howe Laboratory and in this, the most fertile environment I ever hope to encounter, I discovered a world of intellectual stimulation that heretofore never existed for me and that I suspect never exists at all for many less fortunate. Research took on dimensions of meaning, excitement, and joy that I woud never have believed possible prior to my Boston migration. Not

only has my experience here been professionably profitable but the personal enrichment has been a joyful and completely unexpected bonus.

"When one works daily very closely with colleagues, it seems many times more difficult to properly and fully express gratitude and, even more important, admiration of those for whom these feelings exist so strongly. I hope that some indication of my attitude toward the Howe Laboratory and its staff is apparent. My indebtedness to all of you is clearly beyond repayment. My pride in being associated with this Laboratory frankly approaches the sinful. My chief concern now is that in the years ahead my contributions to basic eye research will in some small part justify my opportunities here."

Texts for Teaching

Continuing to probe the role of programmed teaching in ophthalmology and encouraged by the success of his previous texts on refraction and on strabismus, Dr. Reinecke has now prepared a third programmed text, this one entitled *Fundamentals of Ophthalmology,* written in collaboration with Dr. Robert Herm. A prototype was tried out on more than 1,000 medical students in eight medical schools with their suggestions incorporated into the final version. A planned modification of this text is to be adapted for computer delivery in conjunction with a series of slide presentations.

Dr. Donaldson completed the second volume in his series of atlases covering external diseases of the eye. The present book encompasses diseases involving the orbit, lacrimal apparatus, lids, and conjunctiva with illustrations from his large collection of stereophotographs.

Library

The Howe Library, a symbiotic appendage of the Laboratory and Infirmary, served its customarily effective role under the guidance of Charles Snyder who reports ". . . we have loaned books, we have bound books, and we have bought books." Noting no important innovation of the past year he comments with reassuring whimsicality that: "Neither have we known any rumbles, riots, sit-ins, or confrontations." Behind these modest comments is a person and a library outstanding for its documentation of the history of ophthalmology and contributive to the bibliographic stature of ophthalmology.

AWARDS, HONORS AND INVITATIONAL LECTURES

The coveted Friedenwald Award, marking the recipient as the outstanding research man of the year in ophthalmology, was granted to Dr. Kuwabara at the annual meeting of the Association for Research in Ophthalmology. In the Friedenwald Lecture, linked to the Award, Dr. Kuwabara reviewed the intricate relationships of neural pathways and of supporting glia, basing his observations on an authoritative familiarity in the histochemical and electron microscopic structure of the retina.

Plaque of the Friedenwald Award received by Dr. Toichiro Kuwabara.

The Japanese American Citizens League awarded Dr. Kinoshita a silver medallion symbolic of distinguished achievement. He was one of four educators to be honored at ceremonies held in California. The Panamerican Society of Ophthalmology presented Dr. Donaldson a citation at its meeting during the sessions of the Academy of Ophthalmology and Otolaryngology.

The Ulmer Award, given at irregular intervals for outstanding achievement to a junior investigator in the Howe Laboratory, was received this past year by Dr. Chylack.

Dr. Cogan received the MacKenzie Medal and gave the MacKenzie Lecture as part of the Centennial in Glasgow commemorating that pioneer in Scottish Ophthalmology for whom the medal was named.

Dr. Grant was awarded the Howe Medal by the American Ophthalmological Society. This high award is given for notable contributions to ophthalmology.

ORGANIZATION

Major administrative changes, presaged in last year's Report, were instituted this year. The Howe Laboratory, the first endowed ophthalmic research laboratory in this country, has had unusual opportunities to explore administrative patterns of organization in the 40 years of its existence. Established as a separate department of the Harvard Medical School, it has for many years been housed at the Infirmary where it has enjoyed a propitious relationship both to the hospital and to the Department of Ophthalmology at the Medical School to which it was naturally allied.

Although research and clinical integration has its virtues, it also has its liabilities, and important to the success of the Howe Laboratory in the past has been its autonomy and its considerable freedom to make its own decisions. Like the ideal marriage partner, it has kept its individuality while serving devotedly the common connubial aims. While pointing, in last year's Report, to the divergent but parallel qualities of the investigator and of the clinician, we expressed concern lest we were failing to respond adequately to the needs of each. We aired the fear that a single Director for all three functions – clinical chief, department head, and research head – might in fact threaten the favorable environment in which research had prospered.

It was with this in mind that Dr. Cogan resigned as Chief of Ophthalmology at the Infirmary so as to spend his time more effectively in research and in teaching. It was then decided at an administrative level that he be replaced as Chairman of the De-

partment at Harvard, on the grounds that the two appointments had been historically linked. Although we are of the persuasion that the Directorship of the Howe Laboratory and the Chairmanship of the Department of Ophthalmology at Harvard would have maintained a more natural liaison, and that a pioneer opportunity in administration has been lost, we cannot help but feel that the change may favor greater development of the research potential of the Howe Laboratory. Hence we are ever more optimistic about the possibilities of its future.

SUPPORT

Although emphasis is placed in this Annual Report on the investigation and on the men doing the work, all of us know that little could be accomplished without the magnanimous support of the many individuals and agencies who have contributed to the Howe Laboratory. If we were to depend on the endowment of the Laboratory, we could support no more than one or at the most two investigators. Our present position, indeed our entire growth and productivity, has been a direct outgrowth of the support which has been given us.

The government through its National Institutes of Health, has been a major source of support. We wish to acknowledge privately, as we have publicly, the exemplary way in which funds are allocated not only to the Howe Laboratory but to all laboratories in accordance with their research potential. The NIH, more specifically the Institute of Neurologic Diseases and Blindness which has been the granting agency, has been a model of non-bureaucratic administration in which several of us from the Howe Laboratory have had the privilege to serve as Council or Section members.

But it would be imprudent to commit a continuing laboratory too heavily to fiscal support which, as we have learned this past year, is subject to severe cut-backs. Our unwritten policy has been to keep government support at about the 50% mark. We are, therefore, extremely grateful for the assistance given by private agencies and individuals who include the Howe Laboratory in their philanthropy.

The Lions Clubs of Massachusetts, long known for their dedi-

cation to eye research, has in recent years contributed substantially to the Howe Laboratory. The pre-eminence which Dr. Kuwabara and the Howe Laboratory have attained for electron microscopy of the eye was made possible to a considerable extent by funds from the local Lions Clubs. Other projects have also been greatly assisted by the Lions this past year including Dr. Taylor Smith's investigations in the Pathological Laboratory and Dr. Wiedman's investigations of retinal embryology. For their continuing support, we are most grateful to the Lions Clubs.

We are also grateful to Genradco Trust, Research to Prevent Blindness and The Devonshire Associates who have made contributions that assisted many pioneer investigations at a pilot stage where seed money was necessary before a definitive project could be launched. Such support has a profound effect on all our operations.

We are no less grateful to the many individuals we are listing who, without solicitation, have contributed to the Howe Laboratory. In the present era of fund-raising pressures, it is heartening to know that a substantial body of benefactors rises above the prevalent euphemisms of salesmanship, to support what they as individual judges choose. We are grateful for the funds and for the spirit in which the funds are given.

Finally we would like to note one contribution to the Laboratory which has particular significance. Two of the resident staff were presented with $1000 by a commercial company for their development of a surgical instrument which this company subsequently produced. Now, residents' salaries are not by any means excessive, but instead of accepting the donation, these residents chose to contribute it to the Howe Laboratory expressing the hope that others might have the same opportunity which they had had.

EPILOGUE

In the year just passed, one that is sure to be identified historically with storms of violence, hypocrisy and confusion, eye research has been a haven for those who have wanted to make a scientific and humanitarian contribution in an orderly manner. Those of us and those of you who have shared in these efforts to understand the eye and its diseases and, hopefully, to alleviate in some measure

the constant threat of blindness, are fortunate. We are fortunate to be able to dedicate our energies and consciences to ends that transcend the unhappy circumstances that have swirled around us.

It is a pleasure in recording the Laboratory's accomplishments to acknowledge the many sources of our help.

David G. Cogan, M.D.
Director

For General Expenses

Individual benefactors

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For Specific Projects

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Glaucoma research
Support of the Vision Information Center

Ayerst Laboratories
Studies of human cataracts

Dr. Bertha Offenbach
Howe Library of Ophthalmology

Alfred P. Sloan Foundation
Basic experimental studies in glaucoma

Smith, Miller & Patch, Inc.
Fluorescein Angiography Exhibit

U.S. Atomic Energy Commission
The carbohydrate metabolism of ocular tissue

U.S. Public Health Service
General Research Support Grant
Center Grant
Ophthalmology Training Grant
Vision Information Center
Pressure regulating mechanisms in glaucoma
Research Career Development Award
Cataracts
Electron microscopy of retinal dehydrogenases
Metabolic histochemistry of the retina
Differentiation of chick retina

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The nature and development of ocular motor control. Conference on Influence of Early Experience on Visual Informal Processing. National Research Council, Committee of Brain Sciences, at Lake Mohonk, New York, October 27–30, 1968.

with Schuknecht, H. F. and Wray, S. H.: Television presentation: Eyes and Ears of the Medical World. American College of Physicians, in Boston, November 11, 1968.

with Guzak, S. V.: Fluorescein angiography and pathology. New England Ophthalmological Society, November 20, 1968.

DONALDSON, D. D.

Infectious diseases involving the eye. Postgraduate Course in Internal Medicine, Massachusetts General Hospital, January 27, 1968.

Obscure conditions involving the anterior chamber angle. Institute of Ophthalmology, in New York City, January 29, 1968.

Lesions of the conjunctiva. Wills Eye Hospital, in Philadelphia, Pennsylvania, March 30, 1968.

Course in Industrial Ophthalmology, Harvard School of Public Health:
- Instrumentation of the ophthalmologist, April 8, 1968.
- Problems in industrial ophthalmology, April 15, 1968.

Conference on Research Problems Connected with Diseases of the Eye, Massachusetts Institute of Technology:
- Problems of visualization and recording of ocular disease, April 16, 1968.
- Instrumentation for controlled determination of visual fields, June 20, 1968.

Differential diagnosis of red eye. New Hampshire Conference on Eye Care, in Concord, New Hampshire, April 21, 1968.

Pathognomonic findings in the eye of systemic diseases. Tumors and cysts of the conjunctiva. University of Toronto, in Toronto, Ontario, April 26, 1968.

Essential iris atrophy and Chandler's syndrome. New England Ophthalmological Society, May 14, 1968.

Degenerative conditions of the iris. Section of Ophthalmology, Yale Medical School, in New Haven, Connecticut, May 17, 1968.

Manifestations of systemic infections as seen in the eye. Infectious Disease Group, Massachusetts General Hospital, June 21, 1968.

Lectures to the Lancaster Courses in Ophthalmology, in Waterville, Maine:
- Neuroanatomy of sensory neuro-ophthalmology, July 22–26, 1968.
- External diseases of the eye, August 16–17, 1968.
- Disease of the anterior segment of the eye, August 19–20, 1968.

Series of lectures on external diseases of the eye. Postgraduate Course, University of Pennsylvania, in Philadelphia, Pennsylvania, August 26–28, 1968.

Lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School:
- Corneal dystrophies and degenerations, September 3, 1968.
- Tumors of the conjunctiva and iris, September 14, 1968.
- Ocular signs in systemic disease, September 19, 1968.
- Neuro-ophthalmology, a series of lectures, September 26–November 12, 1968.

Phakomatoses. Dermatology Residents, Massachusetts General Hospital, September 17, 1968.

Systemic diseases and iatrogenic conditions of the cornea. American Association of Ophthalmology and Otolaryngology, in Chicago, Illinois, October 25, 1968.

Blowout fractures in pediatric practice. Pediatric Residents, Massachusetts General Hospital, November 18, 1968.

Problems of anesthesia in blowout fracture. Anesthesia Staff, Massachusetts Eye and Ear Infirmary, December 4, 1968.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
- Blowout fracture, May 16, 1968.
- Diagnosis and treatment of various types of iris atrophy, September 24, 1968.

Fricker, S. J.

Electrical diagnosis of the malfunctioning retina. New England Ophthalmological Society, May 14, 1968.

Electrophysiology. Postgraduate Course in Ophthalmology, Harvard Medical School, September 16 and 17, 1968.

Grant, W. M.

Research problems in glaucoma. Conference on Research Problems Connected with Diseases of the Eye, Massachusetts Institute of Technology, April 16, 1968.

Ophthalmic toxicology. Alumni Association of the Massachusetts Eye and Ear Infirmary, May 12, 1968.

Drugs in ophthalmology. Department of Anesthesiology, Massachusetts Eye and Ear Infirmary, May 22, 1968.

House Officer Lectures, Massachusetts Eye and Ear Infirmary: Childhood glaucoma, June 11, 1968.
The trabecular meshwork, November 26, 1968.

Lectures to the Third Year Class, Harvard Medical School, September 20 and 27, 1968.

Postgraduate Course in Ophthalmology, Harvard Medical School: Tonography and tonometry, September 16, 1968.
Toxicology, September 23, 1968.
Glaucoma, November 13, 1968.

Lectures to the Department of Pharmacology, Harvard Medical School, October 8, 15, 22, 1968.

Distinguishing the different types of glaucoma. Department of Ophthalmology, Boston University Medical Center, November 7, 1968.

Guzak, S. V.

Fluorangiography. Postgraduate Course in Ophthalmology, Harvard Medical School, October 11, 1968.

Jedziniak, J. A.

Aldose reductase from lens and liver. Association for Research in Ophthalmology, in Tampa, Florida, April 29, 1968.

Lens aldose reductase. International Symposium on the Biochemistry of the Eye, in Nijmegen, The Netherlands, June 25, 1968.

Kinoshita, J. H.

Galactosemic cataracts. Diabetes Field Unit, Public Health Service, in Boston, January 25, 1968.

Effects of galactose on the ocular lens. Research Laboratories of the McLean Hospital, in Belmont, Massachusetts, March 6, 1968.

Biochemical aspects of cataracts and retinal disorders. Merck Company, in Rahway, New Jersey, March 15, 1968.

Galactose effects on the lens amino acids. Association for Research in Ophthalmology, in Tampa, Florida, April 30, 1968.

The ocular lens. Conference on the Research Problems Concerned with Diseases of the Eye, Massachusetts Institute of Technology, May 8, 1968.

Sugar cataracts. Department of Ophthalmology, Boston University Medical School, May 9, 1968.

Ophthalmic Biochemistry. Alumni Association of the Massachusetts Eye and Ear Infirmary, May 12, 1968.

Galactosemia. Pediatrics Conference, Massachusetts General Hospital, May 28, 1968.

Series of lectures on ophthalmic biochemistry. Lancaster Courses in Ophthalmology, in Waterville, Maine, July 13–15, 1968.

Series of lectures on ophthalmic biochemistry. Postgraduate Course in Ophthalmology, Harvard Medical School, September 5–10, 1968.

Presentation of the Proctor Award to Dr. A. Pirie. Association for Research in Ophthalmology, in Chicago, Illinois, October 25, 1968.

KUWABARA, T.

Ocular pathology of diabetes. New England Deaconess Hospital, January 12, 1968.

Structure and ultrastructure of the optic nerve. New England Ophthalmological Society, January 17, 1968.

Anatomy and pathology of the eye. Series of lectures to the Fourth Year Class, Harvard Medical School, January–February 1968.

Photoreceptic organ, its membranous structure. Electron Microscopy Seminar, Massachusetts General Hospital, February 5, 1968.

Lysosome and pathology. E.N.T. Research Seminar, Massachusetts Eye and Ear Infirmary, February 19, 1968.

Lipogenesis. Pathology Department Research Seminar, Peter Bent Brigham Hospital, February 28, 1968.

Association for Research in Ophthalmology, in New York City, March 8, 1968:

Structure of developing optic nerve.

with Slansky, H.: Intraepithelial uric acid crystals in the cornea.

Structure of the retina. Neurological Institute, McGill Medical Center, in Montreal, Quebec, April 10, 1968.

Basic science of ophthalmology. Series of lectures, Ottawa University Medical School, in Ottawa, Ontario, April 11–13, 1968.

Vascular changes in diabetes. Pathology Department, Massachusetts General Hospital, April 15, 1968.

Fine structural pathology of the retina. The Friedenwald Lecture. Association for Research in Ophthalmology, in Tampa, Florida, May 1, 1968.

Light damage of the retina. Northeast Photobiology Meeting, in Cambridge, May 10, 1968.

Pathology of the eye in fine structural level. Symposium on Ophthalmic Research, Alumni Association of the Massachusetts Eye and Ear Infirmary, May 12, 1968.

Ultrastructure of the eye. Lancaster Courses in Ophthalmology, in Waterville, Maine, July 6–9, 1968.

Structure of the ocular tissue. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, September–October, 1968.

Pathology of retinal vasculature. Department of Ophthalmology, Vanderbilt University, in Nashville, Tennessee, September 19, 1968.

Ultrastructural changes of the light damaged retina. Retina Society Meeting, in Swampscott, Massachusetts, September 27, 1968.

Structure of the eye. New England Society of Electron Microscopy, in Boston, October 8, 1968.

Diabetic vascular change of the retina. Department of Ophthalmology, Boston University Medical School, October 19, 1968.

with Lessell, S.: Pathological changes in the ciliary muscle of the glaucoma monkey. Association for Research in Ophthalmology, in Chicago, Illinois, October 24, 1968.

Pathology of the cornea. American Academy of Ophthalmology and Otolaryngology, in Chicago, Illinois, October 29, 1968.

Light damage of the retina. Conference on Laser Damage, Boston University Medical School, November 14, 1968.

Laser treatment and retinal vasculature. New England Ophthalmological Society, November 20, 1968.

Pathological finding of laser treated monkey retina. Elliott P. Joslin Research Laboratory, in Boston, December 3, 1968.

LAMBERT, B. W.

The effect of ionizing irradiation on the cation permeability of phospholipid structure. Association for Research in Ophthalmology, in Tampa, Florida, April 29, 1968.

MICHON, J., JR.

with Lambert, B.: The effect of chlorpromazine on the lens. Association for Research in Ophthalmology, in Tampa, Florida, April 30, 1968.

Discussion of the paper "Rabbit lens uptake of tritium-labeled phospholine iodide," by Heskel Haddad and Irving Leopold. Association for Research in Ophthalmology, in Tampa, Florida, April 30, 1968.

The blood-retina barrier. Alumni Association of the Massachusetts Eye and Ear Infirmary, May 12, 1968.

NESBURN, A. B.

Virology of the eye with special reference to treatment of keratitis. New England Ophthalmological Society, April 17, 1968.

with Kibrick, S., Elliott, J. H. and Leibowitz, H. M.: Attempts at inducing reactivation of herpes simplex virus (HSV). Association for Research in Ophthalmology, in Tampa, Florida, April 29, 1968.

Postgraduate Course in Ophthalmology, Harvard Medical School, September–October, 1968.

Basic virology for ophthalmologists.

Clinical evaluation and treatment of viral ocular diseases.

PAVAN-LANGSTON, D.

Chronology of primary herpes simplex infection of the eye and adnexal glands. Association for Research in Ophthalmology, in New York City, March 7, 1968.

Chronology of primary herpes simplex infection of the eye and adnexal glands. Association for Research in Ophthalmology, in Tampa, Florida, April 29, 1968.

Laboratory diagnosis of ophthalmic viral disease. Postgraduate Course in Ophthalmology, Harvard Medical School, October 3, 1968.

Viruses in external ocular disease. Cornea Group, Massachusetts Eye and Ear Infirmary, December 6, 1968.

REINECKE, R. D.

Ocular motility problems in everyday practice. Northeastern Eye, Ear, Nose and Throat Association, in Schenectady, New York, January 4, 1968.

Silicone lacrimal tube implantation. Nashville Ophthalmologists, in Nashville, Tennessee, January 29, 1968.

Squints and the AC:A nomogram. Vanderbilt Eye Residents, in Nashville, Tennessee, January 29, 1968.

Eye difficulties and reading problems: Report of the Charlestown Project. Association for Children's Learning Disabilities, in Boston, February 3, 1968.

Computer assisted instruction in medical education. Office of Naval Research, ENTELEK, in Cambridge, February 14, 1968.

Basic squint: Diagnosis and operations. Department of Anesthesiology, Massachusetts Eye and Ear Infirmary, February 21, 1968.

Chronic temporal arteritis — an unrecognized entity. Association for Research in Ophthalmology, in Tampa, Florida, April 29, 1968.

Vision Information Center. American Foundation for the Blind, Conference on Documentation and Information Retrieval in Human Sensory Processes, in Pittsburgh, Pennsylvania, June 13, 1968.

Chronic temporal arteritis — consecutive biopsies and electron microscopy. American Medical Association, in San Francisco, California, June 16–20, 1968.

Pediatric ophthalmology. Nursing Service, Massachusetts Eye and Ear Infirmary, May 9, 1968.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
Treatment of epiphora, July 23, 1968.
Surgical management of chronic dacryocystitis: Movie. October 1, 1968.

Temporal arteritis. Staff Conference, Robert Breck Brigham Hospital, July 25, 1968.

Silicone lacrimal tube implantation. American Academy of Ophthalmology and Otolaryngology, in Chicago, Illinois, October 1968.

New England Ophthalmological Society, December 18, 1968:
Symposium on strabismus: Case presentations.
Random dot stereoscopic patterns of the illiterate E.

SNYDER, C.

Case No. 682. New England Ophthalmological Society, May 14, 1968.

The literature of ophthalmology and how to use it. Postgraduate Course in Ophthalmology, Harvard Medical School, September 5, 1968.

The Massachusetts Charitable Eye and Ear Infirmary: 1824–1864. House Officer Lecture, Massachusetts Eye and Ear Infirmary, November 7, 1968.

STAMPFER, K.

Light damage on the pigment epithelium. Association for Research in Ophthalmology, in New York City, March 8, 1968.

WEIDMAN, T. A.

Prenatal development of the rat retina. Association for Research in Ophthalmology, in Tampa, Florida, April 29, 1968.

Embryology of the eye. Alumni Association of the Massachusetts Eye and Ear Infirmary, May 12, 1968.

WORTHEN, D. M.

Pathology and anatomy. Lectures to the Orthoptics Students, Simmons College, January and February, 1968.

Pathology and anatomy. Two lectures to the Nursing Department of the Massachusetts Eye and Ear Infirmary, during 1968.

Evaluation of cataract cryoextraction. Society for Cryo-ophthalmology, in Miami, Florida, January 17, 1968.

An evaluation of cataract cryoextraction. Eye Staff, Vanderbilt University, in Nashville, Tennessee, May 3, 1968.

Emergency treatment of ocular disease. Emergency Room Staff, Peter Bent Brigham Hospital. Series of lectures, every two months during 1968.

Essentials of the ocular examination. Second Year Class, Harvard Medical School, September 20 and 27, 1968.

Panelist in a forum concerning the impact of Medicare on ophthalmic training and research. National Committee for Research in Ophthalmology and Blindness, in Chicago, Illinois, October 26, 1968.

Pathology and anatomy. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, during 1968.

External eye disease. Series of lectures to the Third Year Class, Harvard Medical School, during 1968.

WRAY, S. H.

The optic nerve. Fourth Year Elective Course, Harvard Medical School, February 16, 1968.

Nerve fiber content and axon branching in the peripheral nerves of the baboon. Department of Neurology, Yale University Medical School, in New Haven, Connecticut, April 16, 1968.

Neuro-ophthalmic evaluation of the patient. House Officer Lecture, Massachusetts Eye and Ear Infirmary, May 28, 1968.

WURSTER, J. B.

Neuro-ophthalmology. Third Year Class Section, Harvard Medical School, December 20, 1968.

EXHIBITS

Wray, S. H., Guzak, S. V., Cogan, D. G. and Lancaster, R. C.
Fluorescein Angiography of the Fundus Oculi. American Academy of Ophthalmology and Otolaryngology, in Chicago, Illinois, October 27–November 1, 1968.

Reinecke, R. D.
Vision Information Center of the Neurological Information Network. American Academy of Ophthalmology and Otolaryngology, in Chicago, Illinois, October 27–November 1, 1968.

FORM OF BEQUEST

The Howe Laboratory of Ophthalmology is an independent department of the Harvard Medical School and is jointly supported by a restricted endowment of Harvard University and by the Massachusetts Eye and Ear Infirmary.

For the information of those who may wish to contribute to this Laboratory, a form of bequest is here set forth:

I Give and Bequeath to the Howe Laboratory of Ophthalmology ..... Dollars To be Applied to the Uses of Said Laboratory.

Such bequests are managed by the Treasurer's Office of Harvard University and are tax deductible. The income is accredited to the Laboratory.

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